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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,544	10/16/2001	Avi J. Ashkenazi	GNE.2630P1C13	5195

35489 7590 06/15/2005

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,544	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/21/02; 3/19/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

1. Claims 1-57 are canceled.

2. Claims 58-63 are pending and under examination.

Information Disclosure Statement

3. The information disclosure statement submitted on 19 March 2002 has been considered by the examiner. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Specification

4. The disclosure is objected to because of the following informalities:

a. The ATCC address on page 372 needs to be updated to: 10801 University Boulevard, Manassas, VA 20110-2209.

b. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 311, line 33. Applicant is required to check the entire disclosure and delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

c. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 58 and 63 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 58 and 63, as written, do not sufficiently distinguish over antibodies that bind SEQ ID NO:523 as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed antibodies and the naturally occurring antibodies. The claimed antibodies read upon antibodies as they are naturally synthesized in eukaryotic cells.

In the absence of the hand of man, the naturally occurring antibodies are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1996)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F. Supp 68 (1967), 155 U.S.P.Q. 139, (District Court, New Jersey, 1967)). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

35 U.S.C. § 112, Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 58 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 58 recites an antibody that binds a polypeptide, whereas claim 63 recites an antibody that *specifically* binds the same polypeptide. Neither the art nor the specification provide a clear definition for, or distinction between, "binds" and "specifically binds". Therefore, the metes and bounds of the claimed invention cannot be determined.

Priority

Applicant claims priority to five previous applications in the preliminary amendment of 03 September 2002. The specification discloses that the claimed polypeptides have patentable utility for the subject matter defined in claims based on the proliferation of rat utricular supporting cells assay (Example 116 at page 347), which was first disclosed in PCT/US99/05028 (WO 99/46281 see page 277), filed 3/8/1999 and the chondrocyte re-differentiation assay (Example 126 at page 351), which was first disclosed in PCT/US00/04341 (WO 00/53756), filed 2/18/2000. Therefore, the claims are granted the filing date of PCT/US99/05028, i.e., 3/8/1999 for purposes of applying the prior art.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 58 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Struyk et al (The Journal of Neuroscience, 15(3):2141-2156, March 1995, Ids reference 12 filed 2/21/02).

The claims are drawn to an antibody that binds or specifically binds the polypeptide of SEQ ID NO:523.

Struyk et al teach a polyclonal antibody that binds, or specifically binds, an isolated polypeptide having a sequence that is 91% identical to SEQ ID NO:523 and 97% identical to the mature form of the polypeptide of SEQ ID NO:523 (i.e., lacks the signal sequence, residues 1-28 of SEQ ID NO:523). See Figure 3 and page 2142, right column and Exhibit A attached to the back of this Office Action. Therefore, it is the Examiner's position that Struyk et al have produced antibodies that bind to the same antigen that the claimed antibodies bind. One of ordinary skill in the art would reasonably conclude that the antibodies of Struyk et al also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Struyk et al have produced antibodies that are identical to the claimed antibody. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibodies of Struyk et al, the

burden of proof is upon the Applicants to show a distinction between the structural and functional characteristics of the claimed antibody and the antibodies of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 58-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Struyk et al (The Journal of Neuroscience, 15(3):2141-2156, March 1995, Ids reference 12 filed 2/21/02) in view of De Boer (U.S. Patent 5,874,082, filed 2/23/1996).

Claims 58 and 63 have been described supra. Claims 59-62 recite wherein the antibody is a monoclonal antibody, a humanized antibody, an antibody fragment and wherein the antibody is labeled.

As discussed above, Struyk et al teach a polyclonal antibody that binds, or specifically binds, an isolated polypeptide having a sequence that is 91% identical to SEQ ID NO:523 and 97% identical to the mature form of the polypeptide of SEQ ID NO:523 (i.e., lacks the signal sequence, residues 1-28 of SEQ ID NO:523). Struyk et al do not teach monoclonal antibodies, humanized antibodies, antibody fragments, or labeled antibodies.

However, such forms of antibodies were routinely made and used in the art at the time of the invention. For example, De Boer discloses these forms of antibodies at column 3, second paragraph and column 7, fourth paragraph.

Therefore, it would have been obvious to one of ordinary skill in the art at the tie of the invention to modify the antibodies taught by Struyk et al such that the antibodies were monoclonal, humanized, fragments and/or labeled as disclosed by De Boer with a reasonable expectation of success. The motivation to do so is given by De Boer, who discloses that humanized monoclonal antibodies are particularly useful in therapeutics,

since there is a lower chance of immune reaction when administered to a human (col. 3, 2nd paragraph), fragments are equivalent to full antibodies (col. 3, 2nd paragraph) and labels are useful for visualization (col. 7, 4th paragraph). One of ordinary skill in the art would reasonably conclude that the antibodies of Struyk et al in view of De Boer also possess the same structural and functional properties as those of the antibodies claimed. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibodies with the antibodies of the prior art, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibodies of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

13. No claim is allowed.

14. Fukushima et al (U.S. patent 6,664,383 B1) has been considered by the examiner, but not applied because the priority date of the instant claims is deemed to be 3/8/1999 (see "Priority" section above). Fukushima teach antibodies that bind a polypeptide (i.e., SEQ ID NO:3) having a sequence identical to SEQ ID NO:523 of the present claims.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
6/10/05

Exhibit A

RESULT 1
I56551
neurotrimin - rat
C;Species: Rattus norvegicus (Norway rat)
C;Date: 26-Jul-1996 #sequence_revision 26-Jul-1996 #text_change 09-Jul-2004
C;Accession: I56551
R;Struyk, A.F.; Canoll, P.D.; Wolfgang, M.J.; Rosen, C.L.; D'Eustachio, P.; Salzer, J.L
J. Neurosci. 15, 2141-2156, 1995
A;Title: Cloning of neurotrimin defines a new subfamily of differentially expressed neu
A;Reference number: I56551; MUID:95198094; PMID:7891157
A;Accession: I56551
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: mRNA
A;Residues: 1-344 <RES>
A;Cross-references: UNIPROT:Q62718; EMBL:U16845; NID:g755184; PIDN:AAA67445.1; PID:g755
C;Superfamily: carcinoembryonic antigen; carcinoembryonic antigen precursor amino-termi

Query Match 90.8%; Score 1639.5; DB 2; Length 344;
Best Local Similarity 92.9%; Pred. No. 2.5e-113;
Matches 312; Conservative 9; Mismatches 12; Indels 3; Gaps 1;

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Qy         12 ISWAIFTGLAALCLP---QGVPVRSGDATFPKAMDNVTVRQGESATLRCTIDNRVTRVAW 68
              : |     ::   ||    ||||||||||||||||||||||||||||||||||||||||
Db          9 LPWKCLVVVSLRLLFLVPTGVPVRSGDATFPKAMDNVTVRQGESATLRCTIDNRVTRVAW 68

Qy         69 LNRSTILYAGNDKWCLDPRVVLLSNTQTQYSIEIQNVDVYDEGPYTCSVQTDNHPKTSRV 128
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         69 LNRSTILYAGNDKWCLDPRVVLLSNTQTQYSIEIQNVDVYDEGPYTCSVQTDNHPKTSRV 128

Qy        129 HLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYLEI 188
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        129 HLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYLEI 188

Qy        189 QGITREQSGDYECSASNDVAAPVVRRVKVTVNYPPYISEAKGTGVPVGQKGTLQCEASAV 248
              |||||||||:|||||||||||||||| ||||||||||||||||||||||||||||||||
Db        189 QGITREQSGEYECSASNDVAAPVVRRVNVTVNYPPYISEAKGTGVPVGQKGTLQCEASAV 248

Qy        249 PSAEFQWYKDDKRLIEGKKGVKVENRPFLSKLIFFNVSEHDYGNYTCVASNKLGHTNASI 308
              |||||||:|||||||:|||||||||||||||:| ||||||||||||||||||||||||||
Db        249 PSAEFQWFKDDKRLVEGKKGVKVENRPFLSRLTFFNVSEHDYGNYTCVASNKLGHTNASI 308

Qy        309 MLFGPGAVSEVSNGTSRRAGCVWLLPLLVLHLLLKF 344
              ||||||||||:|||||||:|||||||||||||||||
Db        309 MLFGPGAVSEVNNGTSRRAGCIWLLPLLVLHLLLKF 344
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